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Hospital for Special Surgery

95th Annual Report

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Report of the Research Director



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Report of the Director of Research

There were two especially important events in the history of the Research Department in 1958. The first was the breaking of ground on the lot at the northeast corner of East 71 Street and the East River Drive, and the beginning of the construction of the new Alfred Caspary Research Building in March. Construction proceeded without interruption during the year, and at the time of this writing (April, 1959), the exterior is practically completed and occupancy is expected towards the end of the year.

The second event was the incorporation of the Philip D. Wilson Research Foundation which is to take over the ownership and operation of the new building. By the terms of incorporation the Members of the Board of Managers of the Society for the Relief of the Ruptured and Crippled are the Members of the Foundation and they in turn are responsible for the election of the Board of Trustees. This Board with a present membership of twenty-three is divided between professional and non-professional people with a controlling vote in case of deadlock on the latter side. At the time of the incorporation a contract was executed between the Hospital for Special Surgery and the Foundation under whose terms the Hospital guaranteed to turn over to the Foundation such funds as it might receive, either from specific research trusts or by direct gifts for the purpose of research in return for the promise of the Foundation to use these funds entirely for research in the field of crippling diseases and in cooperation with the members of the clinical staff of the Hospital.

The origin of this Foundation is attributable to a gift from Mrs. Carolyn Coe of \$350,000 towards the completion of the building which was made subject to certain conditions. It was decided that these conditions could best be met by the creation of this Foundation. Mrs. Coe is the widow of the late William R. Coe who left a generous legacy to the Hospital in the form of a trust fund whose income was to be used exclusively for research. It is felt that apart from the benefit of qualifying for the above gift the setting up of this Foundation will bring other benefits in the way of clarifying the direction of fundamental research and also in the management of funds given entirely for the purpose of research.

The Research Department suffered also a great loss in 1958 in the resignation of its Committee Chairman, Mr. S. Hazard Gillespie, Jr. who since 1955 had been most diligent in conducting its affairs. Mr. Earl Osborn was appointed to replace him.

Financial

While the progress of research in a department such as ours is dependent upon the activity of the scientific investigators who are appointed to its staff or to the efforts of the clinicians of the Hospital staff who receive its support, nevertheless the extent of their activities is in the last analysis based upon the amount of financial aid which can be given them. Research procedures today are complicated and require not only expensive material and equipment but also the technical help of many skilled persons whose annual salaries add up to a large sum. For this reason statements of income and expenditure are always important in reports of Directors of Research.

Research Departments never have enough income to do as much work as their investigators would like to do and therefore are always seeking to find additional sources of funds. While in the new Era of Research large amounts of funds are available for support of research from the National Institutes of Health or other Federal Agencies, or in the form of grants from Private Foundations, these grants never cover the salaries of the principal investigators or of their chief assistants and only occasionally pay the cost of expensive equipment needed for the study. The amounts allowed in these grants for overhead costs of the Research Department or Institute are estimated on a percentage basis and are always too small to cover more than a small part of the actual overhead cost. This is true to such an extent that often-times an institution has to pause and consider whether it can afford to apply for a grant for a research project which it is desirous of carrying out.

A statement of the financial operations of the Department is published elsewhere in this report and comment here will be restricted to a few points. Our income is largely derived from the Bicknell and Coe Trust Funds and from such gifts and donations as may be given directly to the Hospital for the purpose of research. As a result of unexpected circumstances which are not likely to be repeated, we received a total income of \$252,827.00 as compared with a budgeted estimate at the beginning of the year of \$178,619.85. Against this we had a total expenditure of \$193,173.83 including equipment bought at the cost of \$52,862.91. We actually ended the year with a surplus of \$52,656.97 which is most welcome as it leaves a sum which may be applied to the budget for 1959 and particularly towards the vast but as yet inestimable cost of equipping the new Research Building. Our grants-in-aid amounted to a total of \$68,927.00 which is small in proportion to the resources of our Department and this amount should be considerably increased during the coming years.

Nonetheless in spite of the report of successful financial operations in 1958 those of us who are responsible for the direction of the research program for the Hospital for Special Surgery face the year 1959 with considerable anxiety. We cannot as yet estimate the cost of the expanded research program which will result from the completion and occupancy of the Alfred Caspary Research Building. We have appointed Robert Mellors, Pathologist of the Hospital to serve as Associate Research Director beginning January 1, 1959. His field of research is Cancer and the Collagen Diseases. We have made commitments to appoint a team of investigators to work with him which will include an Assistant Patholo-

gist and Electron Microscopist, a Microbiologist and an Immunologist. This is only a sample of the way our work may expand in the new building. We want to be able to staff our laboratories and we must be able to snatch top-notch investigators when they come along. In our employment procedures we follow the policy that second best is never good enough and only the best will do.

Appointments

The following appointments were made during the year:

Jacques Gascon, M.D., Research Fellow in Rheumatic Diseases, July 1, 1958 to July 1, 1959.

William Arnold, M.D., Orthopedic Research Fellow, April 1, 1958 to April 1, 1961.

Robert Tate, M.D., Junior Orthopedic Research Fellow, July 1, 1958 to July 1, 1959.

Russell Gee, M.D., Orthopedic Research Fellow, January 1, 1959 to January 1, 1962.

Leonard Korngold, Ph.D., Immunologist, effective July 1, 1959.

Fred Rapp, Ph.D., Microbiologist, effective July 1, 1959.

James C. Harkin, M.D., Assistant Pathologist and Electron-Microscopist, effective July 1, 1959.

J. Paul Harvey, Jr., M.D., Renewal of appointment as Orthopedic Research Fellow, January 1, 1958 to December 31, 1958.

The list of members of the research staff is listed on one of the following pages.

Research Projects (Clinical)

Research projects are undertaken by members of the clinical staff of the Hospital, sometimes with the assistance of investigators in the basic science laboratories and sometimes not. Since we began the operation of the Research Department in 1955 as a separate administrative unit we have registered 49 Research projects and of these 22 have been completed, 7 were terminated for various reasons without being done and 20 are continuing. During 1958 there were registered 12 new projects and of these 4 have been completed and 8 are continuing. Reports on the progress of these works are given at the end of this report.

Research in the Basic Sciences

We maintain laboratories in various basic medical sciences each with its own experienced chief investigator. Some of these are working in grant supported projects; others are supported by institutional funds. Some of these are working in cooperation with clinical

investigators in which case their projects are numbered and their work is included in the following reports of progress. Others are not so included and this work will now be reported as follows:

1. LABORATORY OF BIOCHEMISTRY — Charles J. Umberger, Ph.D., Director; Frank Fiorese, Ph.D., and Giovanni Marsigli, M.D.

This Research Laboratory was crowded out of present accommodations by the need of expanding the clinical laboratory facilities of the Hospital following the appointment of Dr. Robert Mellors as Pathologist and Director of Laboratories January 1, 1958. Due to the efforts of Dr. Umberger to whom we owe great thanks we were able to find temporary facilities in the basement of the Health Department Facility on East 69th Street not too far from the Hospital and we transferred equipment there and established a temporary laboratory where the research can be carried on without too great handicap. Nevertheless we are looking forward to the reorganization of this laboratory in the new building. The work of this Laboratory is reported in 2-52-O.

2. LABORATORY OF HISTOCYTOCHEMISTRY — Edgar Tonna, Ph.D., Director

Dr. Tonna has continued his study of the activity of the osteoblasts of the periosteum of rats at varying ages and his report of progress will be found in Project Report 4-55-HC.

3. LABORATORY OF MINERAL METABOLISM — Felix Bronner, Ph.D., Director

Some of Dr. Bronner's studies have direct clinical relations with regards to osteoporosis and loss of minerals from the skeleton and these are reported in Projects Reports 42-58-O and 43-58-O. Other studies are of an experimental nature and are reported here.

a) Studies in parathyroid physiology:

Work involving a large number of immature (31 day old) rats has shown that the administration of parathyroid hormone to intact animals will cause excretion in the urine of calcium that had most recently been deposited in the skeletal system. It appears that resorption of the bone salts proceeds along the same route by which the bone salts are deposited. This was demonstrated by showing that the ratio (Ca-45 content of the bone ends: Ca-45 content of bone shaft) was consistently higher in the animals treated with parathyroid extract. In a double labelling experiment in which rats received Ca-45 when they were one month of age, and Sr-85 when they were three months of age, followed immediately by treatment with parathyroid extract, a greater proportion of the more recently deposited isotope was mobilized than of the isotope that had been deposited some weeks previously. This conclusion was confirmed in another experiment in which Sr-85 was given to one month old rats and Ca-45 to the rats when they were three months old. Although it has not been possible to demonstrate that the administration of parathyroid extract affects calcium absorption, the data suggest a shift of calcium throughout the soft tissues, as for example, a rise in liver calcium. All of these findings are consistent with

the suggestion that parathyroid extract promotes the release of calcium from the skeleton in a sequential manner, the most labile calcium being removed first.

b) Kinetic studies of renal handling of calcium:

Studies in dogs, carried out in collaboration with Dr. David D. Thompson, of Cornell University Medical College, have shown that calcium, like sodium, is not only filtered at the glomerulus, but that it also enters the renal tubule by some other path. This was demonstrated by studies in which the rate of appearance in the urine of arterially injected Ca-45 was compared with the rate of arterially injected creatinine, which is a substance known to be neither absorbed nor secreted by the kidney tubules. Phosphate was found to be handled somewhat similarly, although its appearance in the urine preceded that of creatinine by less time than that of calcium or sodium. In general, strontium, sodium, and calcium behaved similarly. Potassium, on the other hand, appeared the earliest of all ions studied and its rate of appearance in the urine was consistent with the possibility that the tubular cells of the kidney in fact secrete this ion. Surprisingly, magnesium behaved as though it were only filtered at the glomerulus without any transtubular component.

This laboratory has now grown to a staff of four technicians, one assistant and a part-time secretary.

During the year Dr. Bronner gave lectures at the Rockefeller Institute and the Gordon Conference on the Chemistry, Structure and Physiology of Bones and Teeth and also participated in a Research Conference on Calcium Requirements and Metabolism in Health and Disease sponsored by the National Dairy Council. He was elected to fellowship in the American Association for the Advancement of Science and to membership in the Orthopedic Research Society and the Biophysics Society.

4. LABORATORY FOR STUDY OF MACROGLOBULINS — Ralph Heimer,
Ph.D., Director

The Director of this laboratory and his staff working in close cooperation with Dr. Freyberg, Chief of the Rheumatic Disease Section has been working intensively on the Separation and Identification of Rheumatoid Factors occurring in the blood serum of patients with rheumatoid arthritis. A report of the progress of their studies follows.

Separation and Identification of Rheumatoid Factors in Blood Serum

Studies on the nature of a component found in the blood of individuals with rheumatoid arthritis are being continued in the Laboratory for Rheumatic Diseases. This component, commonly known as the Rheumatoid factor, is the object of intense research in this country and abroad, as its specificity for individuals with rheumatoid arthritis seems to hold the promise of a factor intimately tied up to either the origin or the progress of this disease.

This factor was shown in our own laboratories not to be merely a single substance, but really a complex of closely related high molecular weight protein molecules. Our studies, carried out on the blood of individual donors, revealed the rheumatoid factors to be present in small quantities, but with an unsuspected variety of physical and chemical

characteristics. On the basis of our studies a hypothesis was proposed which claims that no two individuals make the same type of rheumatoid factors. This hypothesis is now being tested by means of painstaking analysis of the isolated materials' molecular dimensions and chemical characteristics.

A proper chemical and physical description of the factors is needed for a number of reasons:

- 1) Little information is available presently concerning the chemistry of these materials.
- 2) Such information might be correlated with data amassed here and elsewhere for deciding whether the rheumatoid factors constitute a unique class of chemical molecules or whether they bear a relationship to other protein material found in the blood.

Comparison of the chemical properties of the rheumatoid factors to similar components of the blood of healthy as well as diseased subjects, may lead to the discovery of the true function of the rheumatoid factor. This in turn could shed light on the nature of the disease process.

As a consequence of present studies, the following seems to be a good working hypothesis.

The rheumatoid factors are not a unique family of high molecular proteins. They resemble in certain respects the proteins found in the blood of individuals having malignancies, liver diseases, syphilis and disorders of the blood. Similarities also exist between the aforementioned proteins and certain naturally occurring antibodies. Some investigators have actually postulated that the rheumatoid factors are antibodies against products of tissue breakdown. In line with such thinking a series of experiments is being conducted in our laboratories designed to test such an antibody hypothesis.

5. LABORATORY FOR STUDY OF CANCER AND CONNECTIVE TISSUE DISEASES — Robert C. Mellors, M.D., Ph.D., Director

Preparations for the organization of this Laboratory in the new Research Building are now being made. Dr. Mellors has assumed his post as Pathologist and Director of Laboratories of the Hospital on a half-time basis. Beginning January, 1959 he will devote full time, the remainder of his time being devoted to Research in the fields of Cancer and the Connective Tissue Diseases. He has been appointed an Associate Director of Research and will have three experienced investigators whose names were previously mentioned working with him. He has been assigned an entire floor of the Research Building as working space.

Research Projects

The following are reports of progress of the various continuing Research Projects.

1-50-R Richard H. Freyberg, M.D., Director

"Investigation of Effects of Pharmaceutical Substances in Rheumatic Diseases"

The research done under this designation is a heterogeneous program chiefly of clinical

investigation in the problems of rheumatic disease. The support for this group of studies is from several anonymous donors to the Fund for Research in Rheumatic Diseases, which was established in the hospital approximately fourteen years ago, and has been continued through repeated donations and some new donations since that time. Originally, this fund supported the laboratory studies done by the investigators in the Rheumatic Disease Department, but this has largely been supported recently by funds from institutional grant of the Education and Research Department of the Hospital, and all of the grant-in-aid from the Public Health Service now supports this laboratory program. Therefore, this laboratory program will not be reported on in this review.

Most of the investigations supported under the designation 1-50-R are evaluations of various medications that are developed by different pharmaceutical houses that have been prepared either as refinements of known beneficial therapeutic agents or as entirely new drugs whose value needs to be determined. Under carefully controlled conditions these new preparations are being evaluated. The studies during the past year have included chiefly the controlled evaluation of different anti-malarial drugs that have been reported to have various degrees of benefit for rheumatoid arthritis and for systemic lupus erythematosus. These results are being summarized for report to be made soon in an appropriate medical journal. Generally, results of our studies have indicated that there is less benefit from these anti-malarial agents for either analgesic value or anti-rheumatic effect than some other investigators have reported. There is, however, rather dependable benefit through means not yet understood in relieving the activity of the syndrome of systemic lupus erythematosus. Some patients who have less severe illness of this type require no corticosteroids when anti-malarials are used in appropriate doses, and those who require corticosteroids need less of this medication when given simultaneously with anti-malarials.

Another group of drugs in which we have been considerably interested is the group of steroid preparations made for intra-articular use. Recently, triamcinolone acetonide has been prepared, and our studies indicate that this has superiority over previously used corticosteroids when injected directly into the joints. It is tolerated very well. It gives increased relief and somewhat more prolonged relief. However, the differences following injection of this new preparation as compared to the previously available preparations are relatively slight, in the order of ten to twenty per cent superiority.

Dr. Gascon during this past year has made a careful study of the incidence, the complications, of osteoporosis in the corticosteroid-treated patients with rheumatoid arthritis, and is summarizing this information for publication. The frequency of osteoporosis with complicating fractures is surprisingly high in this corticosteroid-treated group of rheumatoid arthritics and presents problems of prophylaxis that will need to be resolved.

This fund has supplemented the salary of one of the Research Fellows. It has paid for various investigations in the clinical and pathologic laboratory of the hospital that are primarily research studies. It has paid for a part-time secretary working with the group of investigators in this department which has no other source for budgetary funds, and transportation of various staff investigators to attend scientific meetings has been paid from this fund for research.

The work done in this category is in my opinion a very important part of the closely

integrated clinical and research program of the department. It is expected to continue indefinitely.

2-52-O Charles J. Umberger, Ph.D., Director

"Biochemical Studies of Stress Induced Urinary Changes"

Experimental work in Bio-chemical Research on post-operative urinary changes has concentrated on clarification of two of the problems initiated in the early part of the investigation.

(1) The question of the origin of trigonelline in the urine as a possible dietary factor has been settled. Studies of the normal excretion under different diets and fasting have shown that the actual urinary concentration is far greater than could possibly occur from ingestion of foods, particularly coffee which has the highest trigonelline content. All evidence indicates that the product is a normal metabolite.

(2) The fact that practically all of the salicylic acid ingested as aspirin is converted to salicyluric acid in the immediate post-operative period has been reported by this group. In normal subjects, the conversion of salicylic to salicyluric acid is variable. In order to complete this work, it is necessary to develop an analytical method for quantitatively determining the concentration of both salicyluric and salicylic acid when both are present as a mixture. Existing methods which require an involved separation of the two components incur considerable error. Two separate procedures for this analysis are under investigation.

4-55-HC Edgar A. Tonna, Ph.D., Director

"Study of the Mitochondrial Variations in Aging Osteoblasts of the Periosteum"

The experiments designed to study the mitochondrial variations in aging osteoblasts have been concluded. The results are in the process of being submitted for publication.

The work revealed that the mitochondrial complement is not only altered by aging but reflects the degree of osteoblastic participation in the production of bone matrix prior to ossification. The changes seen in mitochondria are paralleled by their rate of respiration. A measure of the respiratory rate of these cells or an evaluation of the status of their mitochondrial complement can be used to estimate the degree of active participation in various processes, e.g., bone growth, remodelling, repair, etc.

A more reliable indication of this participation would be expected from measurements of the very enzyme which is responsible for the final liberation of the energy required to carry out these processes (adenosine triphosphatase). Methods have recently become available for the detection and measurement of this enzyme at a cellular level. At present no work has been reported dealing with the skeletal system and ATPase activity. Preliminary work has been started to demonstrate the distribution, abundance and localization of ATPase, and to study the role of this enzyme during bone and cartilage formation at various ages.

7-55-O Jerome Lawrence, M.D.

"Study of the Viability and Survival of Embryonic Joint Cartilage with Reference to Possible Transplantation"

The investigator reports that he hopes to continue with this project, but that at present he is unable to find sufficient time. It is therefore being deferred for a year.

8-55-O Preston A. Wade, M.D., and Robert L. Patterson, M.D., Combined Fracture Service of the New York Hospital and the Hospital for Special Surgery

"Comprehensive Follow-up Study of Patients who have Undergone Bone Fractures and other Skeletal Injuries with Relation to Teaching and Improved Methods of Treatment"

Dr. Robert L. Patterson and Dr. Preston A. Wade, with the assistance of Dr. Paul W. Braunstein, Dr. Rolla D. Campbell, Jr., Dr. Howard Balensweig and Dr. Peter Marchisello — these six members of the Staff — have continued the study of the traumatized patient.

We have continued to receive ambulance cases from Beth David Hospital, Roosevelt Hospital and Knickerbocker Hospital, so that the clinical material has continued to be quite satisfactory.

The Third Annual Postgraduate Course on Trauma was given in June and was well received, there being 51 sessions during the week and 87 surgeons attending the sessions.

The text book "Surgery of Trauma" will be published before June, in time for the A.M.A. meeting at Atlantic City and in time for the Fourth Annual Course on Fractures and Other Trauma. The manuscript went to the publisher on January 9th. Much of the photography, X-ray reproduction and artists' drawings was supported by the Fracture Service.

Dr. Paul Skudder, who was added to the Staff of the New York Hospital in charge of the Emergency Room on July 1, 1958, is working closely with the Fracture Service. He is on a fellowship partially supported by the hospital and partially supported by the Automotive Crash Research Fund under the direction of the Department of Hygiene and Public Health at Cornell. His work is also partially supported by the American College of Surgeons. The Trauma Committee of the American College of Surgeons has initiated a study of Emergency Room care of the injured patient and will use the work done by Dr. Skudder at the New York Hospital as a pilot study. From the first of the year Dr. Skudder will study all cases admitted to the New York Hospital and will then, in the second phase of the work, add other hospitals in the country. Drs. Rolla Campbell, Paul Braunstein and Preston A. Wade presented four papers at the meeting of the Association of Trauma. The work of Dr. Braunstein was a report of experimental investigation of the circulation of the femoral head in dogs after section of the femoral neck. He, also, with Mr. John O. Moore, presented a paper entitled "The Fallacy of Whiplash Injury in the Neck". Dr. Wade presented a paper on Supracondylar Fractures, and Dr. Wade and Dr. Campbell presented a paper on Intertrochanteric Fractures. We are continuing the inves-

tigation of femoral head circulation and Dr. Braunstein, in association with Dr. John W. Draper, has entered upon an experimental project involving bone healing.

The weekly Tuesday evening Fracture Conferences have been well attended and will be continued throughout the year.

13-56-CP William Cooper, M.D.

"Investigations in the Field of Cerebral Palsy"

1. Standard clinical records, employing the forms previously submitted, have been completed on practically all patients in the Cerebral Palsy Clinic. Data contained in the records has been coded and transferred to McBee sorting cards in 1000 cases (500 from the Cerebral Palsy Clinic, and a matching 500 from the Roosevelt Cerebral Palsy Center).

2. Analysis of the data has been carried out in detail. The portion dealing with *prognosis in cerebral palsy* will be presented at the American Orthopaedic Association meeting, and has been submitted for publication in the Journal of Bone and Joint Surgery.

3. A grant of \$2500.00 has been assigned to the Eye Department of New York Hospital at our request for a joint study on *ocular problems in cerebral palsy*. (Grant by United Cerebral Palsy Associations).

4. A movie is being prepared (with the aid of funds from the Department of Health) on *Management of Cerebral Palsy in a Modified Environment*.

17-56-O L. Ramsay Straub, M.D., Secretary, Committee on Training of Orthopaedic Residents. Educational Grant

This project has provided funds to pay the tuition (\$250 per resident) for the Residents to take Dr. Jaffe's special course in Bone and Soft Tissue Pathology. This has been an invaluable experience for each of the men. It has provided training to the following residents and fellows this year:

Dr. Harlan C. Amstutz

Dr. Charles R. Dunbar

Dr. Patrick J. Barry

Dr. Wm. D. Graham

18-56-R Russell L. Cecil, M.D., and Wm. H. Kammerer, M.D.

"Follow-up Study in Rheumatoid Arthritis"

This is to report on Research Project 18-56-R — a long term follow-up of Rheumatoid Arthritis. Two hundred random-selected cases have been studied. All those living have been traced and most have been interviewed and examined. Dr. Donald Mainland, the biostatistician associated with the project, is reviewing the data and through his public health connections is securing the cause of death from various Departments of Health throughout the country on some thirty-six patients who have died. It is anticipated that this work will be in manuscript form in the Fall.

19-56-O Lewis Clark Wagner, M.D., and Associates

"Wedge Osteotomy of the Neck of the Femur in Advanced Cases of Displaced Upper Femoral Epiphysis"

This review has been completed and the author is preparing his material for publication in the near future.

20-56-O Philip D. Wilson, Jr., M.D., Director

"Experimental Production of Scoliosis and Study of Vertebral Growth in Young Animals"

This study has been in abeyance during the last year pending the opening of the new building and facilities for study on a greater variety of animals.

22-56-O Victor Mayer, M.D., and H. Eichenwald, M.D.

"Osteoid Osteoma, Etiological Investigation by means of Viral Techniques"

Since the onset of this project, 11 specimens have been examined for viral agents. Of these, 9 were bone and 2 were blood samples. Of the 2 latter, one blood sample was in a young girl, who we had hoped would progressively demonstrate osteoid osteoma, because of symptoms which so closely resembled, but as yet, this has not been established. Of the bone specimens, at least 2 have not been confirmed pathologically demonstrating osteoid osteoma.

All the specimens were tested against human amniotic epithelial cells in tissue culture and were observed for prolonged periods, extending up to three months. In addition, one half of the specimens were tested against "hela" cells, as well as, monkey kidney, human liver cells and human fibroblasts. Three specimens were tested against chick embryo with a possibility of the bone anlage in the embryo acting as a better medium for growth. In general, centrifugation was done and supernatant fluids used.

Three specimens were injected into cortisone pre-treated mice and rabbits. This was done subcutaneously, intracerebrally and intravenously. Following autopsy of the animals, specimens of brain, bone from the femur, vertebra and skull, liver, fat and kidney were then taken and used for test against human amniotic epithelial cells. The use of the cortisone pre-treated mice was done because in this instance, the mice become extremely susceptible to viral agents.

It has also come to our attention that another laboratory in Boston has also been trying to culture aviral agent from osteoid osteoma during the past year.

In summarization, as yet, no positive growth has been obtained nor any suggestive indication of growth.

It is proposed to continue in the future with new specimens and again continue with viral cultures, utilizing various media which are available since there are so many known factors, which may be present both from the host standpoint, as well as, the medias used for growth. It is felt that it would be wise to continue the present efforts, in spite of negative results, since notoriously, the viral cultures are extremely difficult. It is also

hoped in the future to expand further use of animals in implantation of the virus and secondary recovery for culture.

23-56-O Victor Mayer, M.D., and Associates

"Problems in the Rehabilitation of Patients with Arthrogryposis Congenita Multiplex"

This review has been completed and it is planned to publish two papers which are now in process of preparation. The first will deal with the Public Health aspects of this condition and the second will report the individual cases and summarize the conclusions.

30-57-O T. Campbell Thompson, M.D., L. Ramsay Straub, M.D., and Philip Granieri, M.D.

"Epiphyseodesis and Treatment of Inequality of Leg Length"

This review has been completed and the results will be presented at the next meeting of the American Orthopedic Association, preliminary to publication.

32-57-O John R. Cobb, M.D., P. D. Wilson, Jr., M.D., and C. Veliskakis, M.D.

"Neurofibromatosis and Scoliosis"

An exhibit showing the results of this study was shown at the meeting of the American Academy of Orthopedic Surgeons in New York in January, 1958. Additional cases are being studied and these results will be added to the previous cases. Additional cases are being followed at the present time. It is expected that the material will be ready for publication in 1959. The exhibit has been further modified and is being presented to the American Medical Association Convention in 1959.

33-57-XR R. Freiburger, M.D., B. Loitman, M.D., and M. Helpern, M.D.

"Osteoid Osteoma"

The paper entitled "Osteoid Osteoma, a Report of 80 Cases" was accepted for publication by the American Journal of Roentgenology, Radium Therapy and Nuclear Medicine in October, 1958, but has not yet been published. The exhibit was shown at the American Roentgen Ray Society and the Cornell Alumni Program in 1958.

35-57-O Bernard Jacobs, M.D.

"Osteosynthesis of Bone by Plastic Cement"

The purpose of this study is to make an experimental trial of fixation of broken bones in animals, by the use of a plastic cement-like substance now released by a commercial manufacturer under the trade name of Ostamer. This is a polyurethane foam-like material which when introduced between the ends of broken bones fixes them solidly together

at the same time forming many fine canals through which it is claimed fracture callus will grow. This substance holds promise of clinical application and we are anxious to learn more about it before clinical trial. Our experiments have been delayed through inability to obtain packaged and sterilized material, but we are anticipating receiving the necessary supply early in 1959.

38-58-O Peter J. Marchisello, M.D.

"Study of Osteogenesis by Tissue Culture Methods"

At the present time, the Tissue Culture Laboratory is in functional operation. It is equipped with the basic material prerequisite in any tissue culture laboratory enabling us to perform basic studies in normal and abnormal conditions related to orthopaedics and rheumatology. The present program is designed to study tissues by first dissociating them into individual cellular components and to try to reorganize these cells into tissues suitable of being restored to their histological type. By controlling the environment physiological changes can be produced in order to favor actual bone growth. Such studies when supplemented with time lapse photography give a clear cut picture of how cells divide and assume their physiological characteristics.

39-58-O James A. Nicholas, M.D., Philip D. Wilson, M.D., and Robert H. Freiburger

"Demineralizing Conditions of the Bone"

The original studies and follow-up data on 105 patients with osteoporosis of the spine and vertebral compression fractures have been reviewed and brought up to date. Interesting material is being assembled which will be presented in a paper before the American Academy of Orthopedic Surgeons in January, 1959. It is also planned to present an exhibit on many of these interesting cases.

40-58-O William Arnold, M.D.

"Orthopedic Disorders of Genetic Origin and Congenital Anomalies"

This project concerned with a study of etiologic factors in club foot has largely been completed. Nearly 100 families were interviewed and the preliminary report was presented to the research society of the Hospital for Special Surgery in February, 1959. At present the material is now being prepared in manuscript form and it is anticipated that it will soon be submitted for publication.

A corollary project for which no funds were requested was concerned with anatomical studies of congenital anomalies. Several of these have now been completed and others will be carried out when the material becomes available. Considerable data upon an anatomical study of a specimen of congenital absence of the fibula has been incorporated into an article on the treatment of congenital absence of the fibula which will be published in a volume of "Clinical Orthopedics" this year.

41-59-O Joseph Moldaver, M.D.

Book on Electromyography and Electro-diagnosis

A book on electrical diagnosis in neuromuscular diseases is in preparation. This will be published by Charles Thomas.

It is intended to cover the different techniques used — that is to say, electrical stimulations of nerves and muscles as well as the field of electromyography.

A grant has been given for the illustrations of the book. These will include drawings and reproductions of photographic recordings of the electromyographic patterns.

This book intends to bring together information useful to the diagnosis of neuromuscular diseases as well as their prognosis.

42-58-O Dr. Felix Bronner, Philip D. Wilson, M.D., James A. Nicholas, M.D., John R. Cobb, M.D., and Philip D. Wilson, Jr., M.D.

"A Study of Demineralization with Special Reference to Scoliosis"

The laboratory has been fortunate in securing substantial support from the Atomic Energy Commission and the National Institutes of Health for the purpose of carrying out clinical studies in osteoporosis. This program required considerable preparation such as new instrumentation, the addition of new personnel, and added laboratory space.

43-58-O Dr. Felix Bronner, Philip D. Wilson, M.D., and James A. Nicholas, M.D.

"Mineral Metabolism in Post-Menopausal Osteoporosis"

In this investigation it is proposed to carry out balance studies in patients with osteoporosis and to check the rate of calcium excretion with use of radio-active calcium-45 and strontium-85. Before beginning on the clinical study, it is proposed to make similar studies on normal volunteer controls, in order to determine normal values. The matter of securing these volunteers has taken considerable time, but plans are now being made to begin these studies early in 1959. Two volunteers representing pre-menopause and post-menopausal ages are to be used. The results on these studies will be reported in 1960.

44-58-CP William Arnold, M.D., and William Cooper, M.D.

"Evaluation of Surgical Treatment in Cerebral Palsy"

This study which is concerned with the results of surgery in cerebral palsy patients is now getting underway. The charts of approximately 100 patients have now been reviewed and a considerable number of these patients seen. It will be necessary to review the records of 2 or 3 hundred more patients and to personally interview another like number. Motion picture studies and gait studies in these patients are being deferred until funds become available. A detailed application for a program grant from the United Cerebral Palsy Foundation has been prepared and submitted to this organization. It is hoped that this will be approved and funds will be available for a more elaborate study of these

patients. However even if the funds are not available and the project is not approved by the United Cerebral Palsy Foundation I believe that a worthwhile study can still be carried out.

46-58-P Robert C. Mellors, Ph.D., M.D.

"Pathologic and Immunologic Studies of Connective-Tissue Diseases"

The articular bones in a joint are held together by a tough fibrous capsule which is lined by a specialized membrane called the synovial membrane. The synovial membrane produces a liquid secretion which is required for the nutrition and the lubrication of the joint surfaces of the articular bones. In rheumatoid arthritis the synovial membrane becomes inflamed, for reasons unknown, and grows over and destroys the joint surfaces of the articular bones. Microscopic examination of sections of the inflamed synovial membrane indicates that there are several varieties of inflammatory cells present. Among these are cells — called plasma cells — which in other locations in the body are known to produce antibodies or immune bodies, such as those that combat bacterial infection. But in rheumatoid arthritis there is no known bacterial infection of the joints so that the presence of the plasma cells must have other significance. It is known, however, that an antibody-like material, the rheumatoid factor, makes its appearance in the blood of patients with rheumatoid arthritis. One of our endeavors is to determine by utilizing a recently developed microscopic procedure where the rheumatoid factor is formed in the tissues, whether in the plasma cells or elsewhere. If we find where the factor is formed we might also, by utilizing similar procedures of study, determine why it is formed and thus gain knowledge of the cause of rheumatoid arthritis.

48-58-P Robert C. Mellors, Ph.D., M.D.

"Study of Etiologic and Pathogenic Mechanisms in Cancer"
(Study of Cause and Characteristics of Cancer)

Cancer is characterized by the growth of a new tissue not normal to the individual. The growth of the cancer tissue is brought about by an endless succession of cell divisions in which each parent cell divides into two daughter cells, these in turn divide into four, and so on until astronomical numbers of cells — now forming a cancer mass — exist. There are two principle ideas concerning how this may be brought about:

1) cancer may be caused by some unknown, internal factor which interferes with the chemical machinery of the cells that ordinarily regulates or controls cell division; and

2) cancer may be caused by the entrance into the cell of some foreign agent (we call it an extrinsic agent) which interferes with the regulatory chemical machinery. Such extrinsic agents, in the form of viruses, are known to cause cancers of certain types in some experimental animals (chickens, rabbits, mice). In view of this fact, the possible role of viruses in the causation of cancer in man commands serious attention. There is, nevertheless, one feature of a virus-induced disease which is lacking in human cancers: there is no evidence that human cancers are transmitted from one individual to another

by contact, as, for example, is the case with measles, chicken pox, and the common cold or the virus-induced cancers in experimental animals, such as leukemia of chickens. In other words, a human cancer virus, if such exists, is not infectious. Recent work carried out in other laboratories with certain nontumor-producing virus suggests, that some viruses may exist in either of two forms: 1) an infectious and chemically complete form, and 2) a noninfectious and chemically incomplete form. Viruses in the incomplete form apparently consist of a chemical substance called nucleic acid which is similar in composition to the chemical materials that regulate or control cell growth and division. It is possible therefore that the entrance into the cell of an extrinsic agent similar to an incomplete or noninfectious virus is the cause of some cancers in experimental animals and in man. Upon the opening of the Caspary Research Building, we will undertake once again under the auspices of the National Cancer Institute our investigative work on viruses and cancer causation because of its fundamental aspects and its possible eventual implications for cancer therapy. This study will be undertaken with Dr. Rapp (a microbiologist and virologist); and it is evident that a nucleoprotein chemist is also much needed in the study group.

49-58-O John B. Sullivan, M.D.

"Induction of Bone in Rats with Extracts of Bovine Bone and Cartilage"

Experiments are being conducted on young rats to attempt to induce ectopic ossification with osseo-mucoprotein and renal pelvis epithelium.

Respectfully submitted,
PHILIP D. WILSON, M.D.
Research Director

**NEW YORK SOCIETY FOR THE RELIEF OF THE
RUPTURED AND CRIPPLED
MAINTAINING THE HOSPITAL FOR SPECIAL SURGERY
MARGARET M. CASPARY CLINIC
DEPARTMENT OF EDUCATION AND RESEARCH
PHILIP D. WILSON RESEARCH FOUNDATION**

**Details of Changes in the Research Funds
During the Year Ended December 31, 1958**

	<i>Total All Funds</i>	<i>Education and Research Fund</i>	<i>U. S. Public Health Grants</i>	<i>Atomic Energy Commission Grant</i>	<i>Other Grants</i>
BALANCE AVAILABLE AT DECEMBER 31, 1957	<u>\$199,644.38</u>	<u>\$168,965.28</u>	<u>\$19,051.95</u>	<u>\$ —</u>	<u>\$ 8,627.15</u>
ADDITIONS:					
Income earned and appropriated	48,094.93	48,094.93			
Gifts and Grants received .	256,102.54	168,789.65	38,585.00	24,151.00	24,576.89
TOTAL ADDITIONS . . .	<u>304,197.47</u>	<u>216,884.58</u>	<u>38,585.00</u>	<u>24,151.00</u>	<u>24,576.89</u>
EXPENDITURES:					
Salaries	123,080.21	96,941.66	23,259.30	2,742.00	137.25
Expenses	33,613.62	27,768.75	3,189.74	835.44	1,819.69
Overhead	36,480.00	32,556.85	2,238.28	1,159.87	525.00
Equipment purchased	52,862.91	42,804.51	938.75	9,119.65	—
TOTAL EXPENDITURES	<u>246,036.74</u>	<u>200,071.79</u>	<u>29,626.07</u>	<u>13,856.96</u>	<u>2,481.94</u>
BALANCE AVAILABLE AT DECEMBER 31, 1958	<u><u>\$254,805.11</u></u>	<u><u>\$185,778.09</u></u>	<u><u>\$28,010.88</u></u>	<u><u>\$10,294.04</u></u>	<u><u>\$30,772.10</u></u>

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